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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 :
C12P 21/00, 21/08, C12N 15/63, 1/11, 1/19, 1/21, 5/10, C07K 16/00, A61K 38/43, 39/00, C07K 14/245, 14/39, 14/435

A3

(11) International Publication Number: **WO 99/41404**

(43) International Publication Date: 19 August 1999 (19.08.99)

(21) International Application Number: PCT/EP99/00945

(22) International Filing Date: 12 February 1999 (12.02.99)

(30) Priority Data:
98102546.3 13 February 1998 (13.02.98) EP

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(81) Designated States: CA, JP, US, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

Published
With international search report.

(88) Date of publication of the international search report:
28 October 1999 (28.10. 99)

(54) Title: NOVEL MEANS AND METHODS FOR THE PREPARATION AND ACTIVATION OF NUCLEOSIDE AND NUCLEOTIDE BASED DRUGS

(57) Abstract

Described are novel means and methods for the preparation and activation of nucleoside and nucleotide based drugs. In particular, a method for the production of a polypeptide having or having enhanced kinase activity for a nucleoside or nucleotide analog is provided and polypeptides obtainable by said method. Described are also polynucleotides and vectors encoding said polypeptide obtainable by the method of the invention as well as to host cells transformed therewith. Furthermore, antibodies against said polypeptide are provided and pharmaceutical and diagnostic compositions as well as kits comprising proteins having kinase activity for a nucleoside or nucleotide analog or their encoding polynucleotides or vectors. Furthermore, the use of the before described proteins, polypeptides, polynucleotides, vectors and antibodies is provided for the preparation of pharmaceutical compositions for treating, preventing and/or delaying a disease related to viral infection or cancer. In addition, a method for identifying inhibitors of nucleoside or nucleotide kinases is described and methods for identifying nucleoside or nucleotide based prodrugs employing the above mentioned polypeptides, polynucleotides, vectors and host cells. Also provided are compounds identifiable by said methods as well as pharmaceutical and diagnostic compositions comprising said inhibitors. Moreover, the use of proteins and polypeptides having nucleoside or nucleotide kinase activity or their encoding polynucleotides or vectors is described for the preparation of nucleoside or nucleotide phosphates or analogs and derivatives thereof.

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INTERNATIONAL SEARCH REPORT

Ir ational Application No
PCT/EP 99/00945

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12P21/00 C12P21/08 C12N15/63 C12N1/11 C12N1/19
C12N1/21 C12N5/10 C07K16/00 A61K38/43 A61K39/00
C07K14/245 C07K14/39 C07K14/435

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C12P C12N C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	A. LAVIE ET AL.: "Structural basis for the efficient phosphorylation of 3'-azidothymidine monophosphate by E. coli thymidylate kinase" PROCEEDINGS OF NATIONAL ACADEMY OF SCIENCES USA, vol. 95, 1998, pages 14045-14050, XP002111243 *see the whole article* --- -/--	1-38

[X] Further documents are listed in the continuation of box C.

[ ] Patent family members are listed in annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
4 August 1999	25/08/1999

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 99/00945

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	A. LAVIE ET AL.: "Crystal structure of yeast thymidylate kinase complexed with the bisubstrate inhibitor TP5A at 2.0 A resolution: implications for catalysis and AZT activation" BIOCHEMISTRY, vol. 37, 1998, pages 3677-3686, XP002111244 *see the whole article*	1-38
Y	A. LAVIE ET AL.: "Structure of thymidyalte kinase reveals the cause behind the limiting step in AZT activation" NATURE STRUCTURE BIOLOGY, vol. 4, no. 8, 1997, pages 601-604, XP002111245 *see the whole article*	1-38
Y	D. HAZUDA ET A. : "Failure of AZT: molecular perspective" NATURE MEDICINE, vol. 3, no. 8, 1997, pages 836-837, XP002111246 *see the whole article*	1-38

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